١ / ١ / 20م

ملخص

pharmacology

Introduction and ANS

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مع تحيات
اللجنة العلمية في الدفعة 35 طب بيشة

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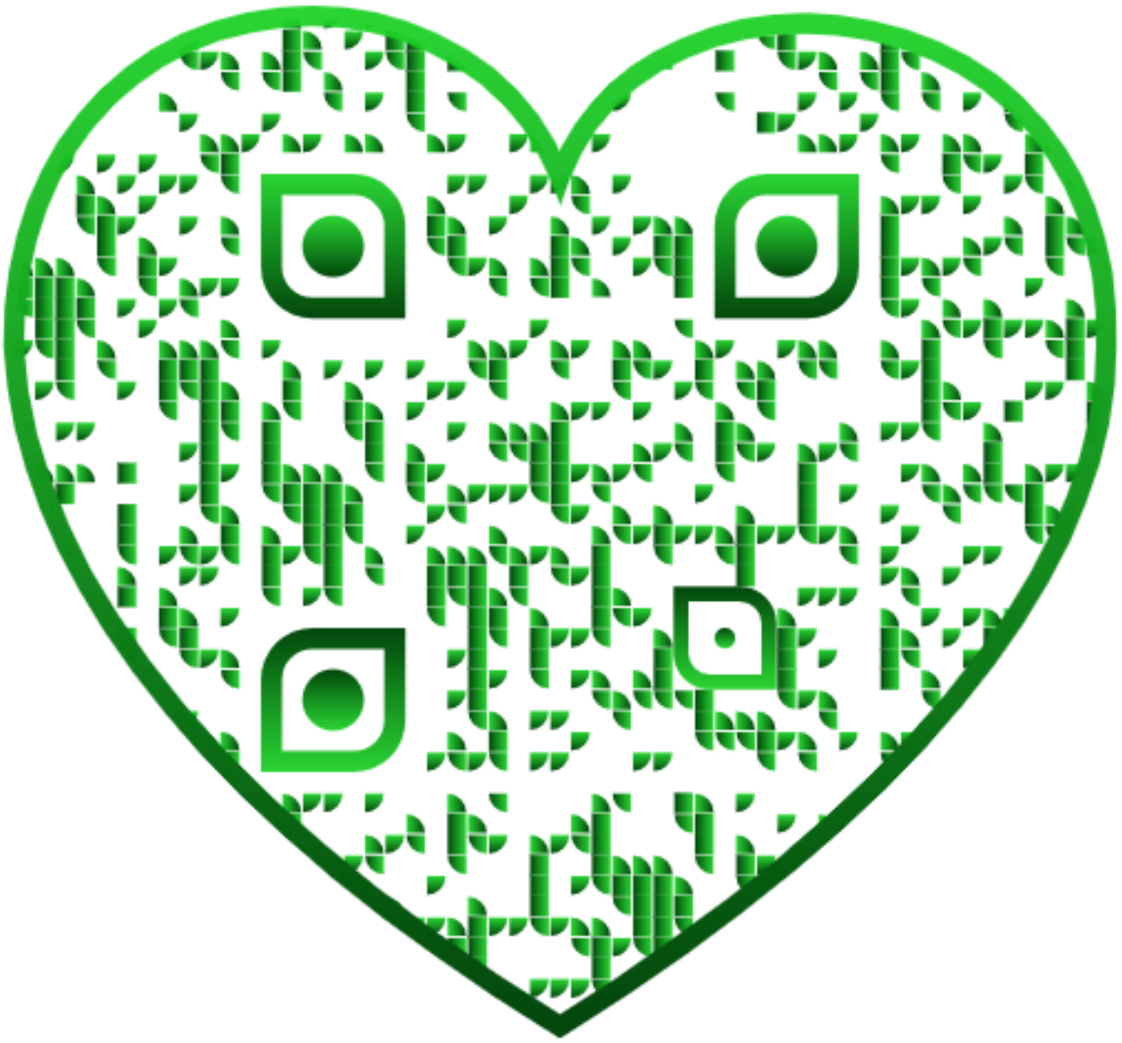

أسماء علوان

2020 / /

1st Lecture — General Pharmacology

Pharmacology: is the science of drug

What is the drug: ⇄ any substance which can alter, treat, Diagnose or prevent disease

Treating → Paracitamol

Prevention → Vaccine

Diagnosis → naloxone for Heroine addiction

→ Edrophonium for myasthenia G.

Sources of drug

Neutral

- From plant → Atropin & hyoscine
- From animal → insulin & heparin
- From microorganism → penicillin
- From marin → Fish liver oil
- From soil → minirals «Zn»

Synthetic

- Represent 90 %
- low coast
- e.g Aspirin

Route of administration

- parentral «iv - id - im - sc»
- oral
  - solid «tablet»
  - liquid «sera»
- topical
  - cream
  - drops
  - ointment
- inhalation
  - general Dru
  - asthma

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sciences of drug

Pharmacokinetic : is the effect of body on drug

Pharmacodynamic : is the effect of drug on the body

Therapeutic use : is the proper choice of drug with proper dose for each situation.

Toxicology : is the study of drug toxicity which include identification of :

- Toxic dose
- symptom of toxic dose
- Antidote.

Note not all drugs overdose are toxic

In pharmacodynamic you should to know:

A : mechanism of action «MOA» B : Pharacological actron

(A) through

- Receptor —e.g→ Adrenalin
- Enzyme —e.g→ Aspirin through cyclo-oxygenase
- Ion channel —e.g→ Lidocaine
- DNA —e.g→ «Anti-viral Drug» mitronidazol
- Chemical reaction —e.g→ Antacid «Hco3» For neutralization
- physical reaction → sucralfate to treat peptic ulcer
  → charchol to oppose toxic dose taken
- cell wall —e.g→ «Anti-Fungal drug» penicillin

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Pharmacological Action

clinical use

side effect

side effect include:

1- Tolerance: is one type of misuse of drug which charactrize by ↑ the dose of drug to get the same effect fo same disease. e.g. using paracetamol for treating h dache after long time you should take more ta to get the same effect.

2- Tachyphylaxis: is the rapid occurance of tolerance

3- Dependent: is severe state of craving in which sudo stop of drug uses may cause central withdr effect e.g Diazepam.

4- Addiction: is severe state of craving in which sud stop of drug use may cause central & perep withdrawal effect. e.g. morphin & Heroin. which leod to many symptom may end by dea

5- Idiosyncrasy: unusual or unexpected side effect of dr due to genetic variation e.g penicillin which cause hypersensitivity reaction.

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2nd Lecture

Pharmakokinetics

Pharmacokinetics: Is the effect of body on the dru

which include

1. Absorption
2. Distribution
3. Metabolism
4. Excretion

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1) Absorption: Transfer of drug from site of administra

to the systemic circulation

Factor affect absorption:-

A: Factor related to drug:

1- solubility: « Lipid soluble sub. more absorped tha

water soluble substance »

2- particle size: « particles will small size is more a

ped than particles with large size.

3- physical propertize « solid - liquid - gas »

« liquid is the best »

4- Ionization: « ↑ polarity ⟶ ↓ absorption

5- dosage form: « taplet - capsule - spray - drop -

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B: Factor related to the patient.

1- Route of administration « entral - topical ... etc »

2- Health state e.g constipation ⟶ ↑ absorption

vomiting & diarrhea ⟶ ↓ absorp

3. Blood Flow

4. presence of food in GIT ⟶ ↓ absorption

Biovailability: is the Fraction of dosed drug that reach

blood circulation = $\frac{\text{conc. of drug in blood}}{\text{dose of drug}}$ x 1

> 80% excellent absorption < 50% poor absorption

e.g: drug dose 500 mg while the amount that absorped is 300 mg

Biovailability = $\frac{300}{500} * 100$ = 60 %

good absorption

2) Distribution: Leaving of drug From systemic circulat to interstitial space of all tissue in the bo

Drug found in Blood circulation in 2 form

Binding Form « inactive » Free Form « active

« Bind to plasma protein mainly albumen »

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3) Metabolism: «the First step of drug elemination »
« is chemical modification of drug structure

- conversion of drug from Lipid soluble to water soluble
  be easily excreted «from active to inactive»
- Convertion of drug From inactive ⟶ active «prodrug» e.g Enalapr
  Active ⟶ Active metabolite e.g Diazepa
  Active ⟶ toxic metabolite e.g paracet
  ↙
  But in chronic use

Factor affect drug metabolism:

★ health state of liver

★ Age « Enzymes more active in young people»

★ Sex « metabolic Rate In male is hieghe than that in Female

★ Drug-Drug interaction

- metabolic inducer
  « drug stimulate metabolism»
  Eg «rifampin-phenytoin»
  whenwe use them with
  warfarin ⟶ ↓ its action
  الكل ليس في زيادة الجرعة وإنما في الفصل بينهما

- metabolic inhibitors.
  « drugs inhibit metabolism»
  E.g « erythromycin - Ritanovi
  when we use them with
  warfarin ⟶ ↑ its effect
  ل ليس بتقليل الجرعة وإنما في الفصل بين
  الدوائين

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4) Excretion: removal of drug outside the body.
depend on healthy state of kidney and liver.

☆ Agonist: drug which bind to receptor and produce biological responce: e.g Adrenergic agonist: drug which bind to adrenegic receptor and produce effect similar to that produced by natural/ neuro-transmitter (adrenalin- nor-adrenalin -Dopamin)

☆ Antagonist: drug which bind to receptors to decrease or oppose effect of another drug or endogenous ligand e.g adrenergic antagonist drug which bind to adrenergic receptor and produce opposite effect to that produced by natural neurotransmitter.

Therapeutic indix (TI): is the degree of drug safiety

$$= \frac{\text{Toxic dose 50}}{\text{effective dose 50}} = \frac{TD50}{ED50} =$$

كلما قلت الـ TI كلما كان الدواء غير آمن

E.g. Drug A: 150 - 50mg ∴ 50 = 20 gm

$$TI = \frac{20000}{500} = 40$$

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* Potency: « the strength of drugs » فعالية الدواء
* Efficiency: maximum responce produced by drugs

- if we have two drugs A = 5 mg B = 100 mg with the same efficiency. drug A will be more potent due to concentration of drug.
- if we have two drugs A = 10 mg B = 10mg But A: wil more high efficiency A will be more efficient.

onest of action of drug: is the duration between admi-ration and appearance of effect of

Duration of action of drug: is the time between onest and end of action of drug.

Estemation of drug responce.

1] disappearance of symptom of disease

2] measuring of parameters مثل قياس نسبة السكر في الدم

3] drug concentration in blood

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3rd Lecture

Drug Affecting ANS

هذه المقارنة لم يشرحها الدكتور وإنما ثوة عليها فقط :

Tissue or organ	sympathetic	parasympathetic
	α-and-β	M_4 & M_5
• CNS	• excitement - learning	• Resting - memory
• Eye	• mydriases α_1	• miosis
	• Relaxation of ciliary m β_2	• contration of ciliary
	• ↑ secretion of aquous humer B_2 fluid	• ↑ drinage of aque humer fluid
• salivary gland	α_1 trophicsecretion	M_3 profuse watary secretion
• heart	B_1 ↑all cardiac properitize	M_2 ↓allcardiac properti
• Blood vessels	α_1 V.C of most B.V B_2 V.D of coronary & B.V in skeletal muscle	
• GIT	B_2 relaxation of wall α_1 contraction of sphencter	M_3 contraction of wall M_3 Relaxation of sphenict
• Lung	B_2 Bronchodilatation α_1 ↓ Bronchial secretion	M_3 Bronchoconstrictio M_3 ↑ Bronchial secreti
• U.B	relaxation of wall contraction of sphencter	contraction of wall Relaxation of spheno
Genetal organ male	Ejaculation	Erection of peni
Female	contraction α_1 Relaxation B_2 of uterus	Erection of clitor

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Drug affecting ANS

★ Parasympathomimetic drug — [Direct, indirect]

★ Parasympatholytic drug

Parasympathomimetic drug

	Direct	indirect
classification		
Examples	pilocarpine	• pyridostigmine • Rivastigmine
MOA	direct stimulation of muscarinic receptor	by inhibition of Ach-esterase enzyme
pharmacological action	similar to Ach.	
side effect	★ Bradycardia ★ hypotension ★ salivation ★ diarrhea ★ dyspepsia ★ abdominal cramps	★ miosis ★ Frequecy of urina ★ Bronchoconstrictio

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- clinical use

1] Glaucoma ((↑ intraocular pressure)) we use pilocarp as eye drop ((↑ drinage of aquous humer fluid))

2] Sjögren syndrom ((is an autoimmune disease in whic the body Form antibodies against lacrimal & salivar gland)) we use pilocarpine and cevimeline

3] myasthena gravis ((autoimmune disease in which the t Form antibodies against nicotinic receptor in neuron cular junction))

تشخيصها عن طريق الطلب من المريض أن يعد الى ٣٠ في البداية ون نبرة صوتية قوية ومن ثم تبدأ بالخفوت تدريجياً

كلمة الوحيدة التي يومئ بها المرض ⟵ Fatiguability

treated by ((Neostigmins & pyridostigmine.

4] Lambert - eaton syndrom ((is an autoimmune disease which the body Form antibodies against voltage gateo Ca^{+2} channel in presynaptic neuron which lead to ↓ release A

تختلف عن myasthena gravis أن الحركة تبدأ بطيئة ومن ثم تزداد تدريجياً

treated by ((pyridostigmine))

5] Alzheimer disease ((loss of recent memory in elderaged

Treated by ⟶ Rivastigmine.

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- contraindication:

☆ Asthma ☆ urinary track obstruction ☆ peptic ulc

Acetylcholine lacks therapeutic importance. why?

Due to ☆ its multiplicity of action leadin to diff
effect « not specific »

☆ its rapid inactivation by the cholinestera

Parasympatholytic « Anti-cholinergic = anti-muscarinic »

- Examdex ☆ Atropine
☆ Hyoscine
} Alkaloid derived from plan

- side effect:

1- Loss of recent memory «amnesia»
2- mydriasis - cycloplegia «paralysis of ciliary muscle
3- dry mouth ← « المريض يتحباش من الحنوء السا طع »
4- dry skin Atropine-like side effect
5- tachy cardia
6- constipation
7- urine retention

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- contraindication

  ✱ glaucoma « because it ↓ drinage of aquous Homer fluid

  ✱ Benign prostatic hyperplesia ((BPH))

Note benign tumer in prostate found in transitional zone whe
malignant tumer found in perephral zone.

- clinical use

  1] Non-infectious diarrhea

  2] severe bradycardia

  3] irreversable Ache(->esterase)se inhibitors poisoning:

  these organophosphorus compound which found in

  Nerve gases : sarin & soman

  insecticide : Malathion & parathion

  « these compound inhibit Ach esterase enzyme by irre
  sable mechanism which lead to ↑ acetyl cholin an
  produce more longer parasympathetic Action as:

  - convulsion
  - Bradycardia → cardiac arrest
  - Bronchoconstriction
  - Frequoncy urination
  - Diarrhea

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All these symptom treated by atropin except convuls

why? Because convulsion occur in skeletal muscle which ha
nicotonic receptor whereas Atropin is antimuscarinic drug

4] Bronchial asthma «Ipratropium»

5] Parkinson's disease « neurological disease caused by decr
dopamine or increasing acetylcholin in basal ganglia.
treated by « procyclidine & Ben2tropine»

6] in operation inorder to ↓ secretions

7] ophthalmological use « for eye examination and treatr
inflammation in iris ~~and~~ choroid, and ciliary body
treated by Atropin or tropicamid

8] urinary incontinence.

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4th Lecture

Drug affecting SNS

Sympathomimetic Drug

Direct

these drug stimulate Adrenergic receptor directly

- α-B agonist
- α agonist
- B agonist
- D agonist

indirect

these drug stimulate release of chatecolamin from presynaptic neurons

- Examples: adrenaline - Dopamine — Amphetamine
- clinical use of sympathomimetic drug:

1) Hypotension and shock

★ in cardiogenic shock

- Dopamine → act on D_1-α_1-β_1 depend on the dose
- Adrenaline — الترتيب حسب الأفضلية
- Nor-adrenalin

Dobutamine also used for treating cardiogenic shock

★ in hypovolemic shock we use nor-adrenaline mainly

★ In anaphylactic shock we use adrenaline mainly

★ Phenylephrine (pure) "α_1 agonist use in vascular shock

we use adrenaline in anaphylactic shock due to it is a physiological anagonist for histamin its dose [0.5 – 1 mg] Taken I.M or I.V.I

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2) Decongestion for ((eye - sinuses - nose - Respiratory)) → Congestion ((vasodilatation))

we use these drug:

* pseudoephedrine
* oxymetazoline
* xylometazoline
* tetrahydrozoline
* Phenylephrine

3) Bronchial asthma

* salbutamol ((Albuterol))
* salmeterol
* metaproternol

} taken by inhalation or injecti

4) prevention of premature labor

* salbutamol ((albuterol)) ⟶ relaxation of uterus

5) Acute heart Failure

* dobutamine
* dopamine
* adrenalin

we do not use Nor-adrenaline due t
it lead to Reflex Bradycardia.

6) with local anesthetic drug ((adrenalin)) why?

Because its v.c effect which prolongate the effect of anesthetic drug by 3 mechanism.

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1- ↓ systemic circulation «localization of drug»

2- ↓ Bleeding

3- ↓ side effect of drug.

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7) ADHD «Attention deficit hyperactivity disorder»

هذا المرض غالباً ما يصيب الأطفال . حيث أن الطفل المصاب يكون نشط بدنياً لأبعد الحدود ولكنه أيضاً بليد ذهنياً لأبعد الحدود

treated by → methylphenidate.

«amphetamine derivative»

Other drug

methyldopa
clonidine
apraclonidine
Tizanidine

} these drug stimulate α_2 receptor in presynaptic neuron and ☆ releasing neuro-transmitter to synaps.

- methyldopa is safe drug for gestetional hypertensio

Mechanis of action → α_2 agonist

→ inhibit chatecolamin formation
«by Formation of false neurotransmitter

methyldopa → methyldopamin → methyl-nor-adren

methyladronaline ←

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- clonidine used for treating ✦ hypertension
  ✦ Addictive symptom after withdrawa
- apraclonidine for treating Glaucoma
- Tizanidine used for treating Spasticity.

LMNL ("lower motor neuron lesion") ⟵ ل ارتخائي

UMNL ("upper motor neuron lesion") ⟵ ل تشنجي

Thalidomide علاج سُحب من السوق بواسطة شركة الصانعة كان يستخدم بكثرة في القرن الماضي ولكن وجدوا أنه يسبب تشوهات في الأجنة حيث أن الأطفال كانوا يولدوا بدون أطراف « Amelia » أو بأطراف حرفية

Are you pregnant or lactating? سؤال مهم قبل وصف الدواء

تقسم الأغذية والأدوية التي تعطى للمرأة الحامل الى ستة مجموعات

Group A Foods لا تأثر على الحمل ولا على الجنين

Group B some drug (penicillin - methyldopa - paracitamol)

Group C علاجات لا تأثر على الجنين

Group D

Group E

Group X علاجات تؤثر على الحمل وتسبب تشوهات في الجنين بنسبة 100%

propranolol does not used for patient with asthma

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Side effect of sympathomimetic drug.

A: Direct sympathomimetic drugs.

- Adrenaline
  - ★ hypertension
  - ★ palpitation
  - ★ tachycardia
  - ★ arrhythmia
- Nor-Adrenaline
  - ★ hypertension
  - ★ reflex Bradycardia
  - ★ not much tachycardia
- Salbutamol
  - ★ hyperglycemia
  - ★ tremor in «tongue & extrimeties»
  - ★ not much tachycardia
- Dobutamine
  - ★ tachycardia
- Dopamine
  - ★ tachycardia
  - ★ hypertension
  - ★ nausia
  - ★ vomiting

B: Indirect sympathomimetic drug

- ↑ ABP
- Tachycardia
- Constipation
- urinary retension
- mydriasis } pere

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Euphoria & Relive of fatigue followed by:

- ★ depression
- ★ anxiety
- ★ insomnia
- ★ Phopia
- ★ tolerance على المدى البعيد

} centrally

- Contraindication:
  - ★ hypertension
  - ★ cardiac arrhythmias

- Drug interaction

  MAOI (mono-Amino- oxidase inhibitor) e.g. tranylcypron

  which ↑ catecholamin and lead to many effec

  → hypertension crisis

  → organ damage

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5th Lecture — Drugs Affecting SNS

Sympatholytics:

- classes
  - α- Blockers
  - β- Blockers
  - α_2- Agonist
  - storage inhibitors

- α-Blockers
  - A: Non selective α-Blaker ((phenoxybenzamine))
  - B : selective α-Blaker . ((Prazosin - tamsulosin))

- therapeutic use of α-Blockers
  1] hypertension ((prazosin)) on α_1
  2] Benign prostatic Hyperplesia ((BPH))
  which charactrized by
    - hesitancy of urination
    - weak urine flow
    - uncomplete emptying of U.B

treated by Tamsulosin which act on α_{1A} and lead to relaxation of neck of U.B & prostate

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3] Pheochromocytoma ((10 % tumer))

tumer in suprarenal ~~medulla~~ medulla. which lea

to ↑ secretion of ~~cate~~catecholamine

~~the~~ skin is pale due to v.c effect of adre

Treated by phenoxybenzamin & propanolol

4] Raynaud's diseasease

((vascular disease which cause numbness & cyano

of the Fingers and toes.

Treated by phenoxybenzamin. But Ca^{++} channel b

is better.

■ side effect of α- Blockers.

- ★ postural hypotension
- ★ Reflex tachycardia ((more with phenoxybenzam

less with prazosin and least with tamsulosin

- ★ nasal stiffness ((congestion).
- ★ myosis المريض لا يستطيع الرؤية في الضوء الخافت

■ Contraindication of α-Blocker:

Hypotension

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- classification: B-Blocker
  - selective
  - Non-selective
- example
  - ✯ atenolol B_1
  - ✯ metoprolol B_1
  - ✯ Bisoprolul B_1
  - ✯ betaxolol B_1
  - ✯ Bytoxomin B_2
  - ✯ propranolol
  - ✯ nadolol
  - ✯ timolol
  - ✯ pindolol
  - (more used clinically)

- clinical use of B-Blocker

1] Hypertension through inhibit B_1 in heard which ✯ all heart propertize and B_1 in Kidney ✯ renin

2] Angina pectoris

3] Cardiac arrhythmia

4] hyperthyrodism (propranolol Better than other dr

5] Glaucoma (timolol & nadolol)

Drug used for treating glaucoma:-

- ✯ pilocarpine
- ✯ apraclonidin
- ✯ CAI (carbonic anhydr)
- ✯ prostaglandin
- ✯ B-Blocker
- (dorsolami

6] prophylaxis of migrain: (propranolol) How?

unKnown (through retrospective studies)

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7] congestive heart failure

« Bisoprolol - Metoprolol - Carvidolol »

8] anexiety

9] portal hypertension

« propranolol but in acute state other drug used

- side effect of B-Blocker.
  - ★ Bradycardia
  - ★ Bronchoconstriction
  - ★ hypoglycemia
  - ★ cold extrimeties
  - ★ Fatigue

- contraindication of B-Blocker
  - Asthma
  - severe bradycardia
  - vasospastic angina
  - perepheral vascular disease
- Drug interaction.

  Ca^{+2} channel blocker which found in B.V & heart e.g { Diltiazem, verapami

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α_2 - Agonists. قد سبق شرحهم

e.g methyldopa

side effect of methyldopa

- ✯ Depression
- ✯ hypotension
- ✯ Bradycardia
- ✯ Parkinson's disease
- ✯ hyperprolactinemia
  - Gynecomastia in Male
  - Disturbances in menstrual cycle in Female

storage inhibitor

Reserpine « Alkaloid drug which inhibit storage of catecholamin so that they degraded by MAO

why catecholamin stored in vesicle?

in order to protet them from MAO & COMT

- therapeutic use

  in hypertension

  in psychosis « side effect of amphetamine »

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